

mixed in the solvent carriers or solutions of materials for electroprocessing. In this system materials can be mixed with various substances and directly electroprocessed. The resulting composition comprising an electroprocessed matrix and substance can be topically applied to a specific site and the substances released from the material as a function of the material undergoing breakdown in the surrounding environment. Substances may also be released from the electroprocessed compositions of the present invention through diffusion.

The state of the electroprocessed material in relation to the incorporated substances is dictated and can be controlled by the chemistry of the system and varies based on the selection of matrix materials, solvent(s) used, and solubility of the matrix materials in those solvents. These parameters can be manipulated to control the release of the substances (or other elements into the surrounding environment). If substances to be incorporated into the electroprocessed material are not miscible with the material, separate solvent reservoirs for the different components can be used. Mixing in such an embodiment occurs prior to, during, and/or after deposition on the target, or a combination thereof. It is to be understood that substances may be entrapped or entangled within an electroprocessed material, bonded to a material before the material undergoes electroprocessing, or bound to specific sites within the matrix material.

In a variation of this embodiment, the substance is a particle or aggregate comprising a matrix of compounds or polymers such as alginate that, in turn, contain one or more compounds that will be released from the electroprocessed material. Drugs can be combined with alginate by, for example, combining a drug suspension or drug particulate in the alginate in the presence of calcium. Alginate is a carbohydrate that forms aggregates when exposed to calcium. the aggregates can be used to trap drugs. The aggregates dissolve over time, releasing the trapped substances, such as cells trapped in alginate. The particles, which are then incorporated within the larger electroprocessed matrix, are biologically compatible but relatively stable and will degrade gradually. In some circumstances, the electroprocessed materials resemble a string of pearls. This is a physical aspect of the electroprocessing. If the polymer concentration is low, electrospraying of beads occurs. As polymer concentration increases there are some beads and some fibers. A further increase in polymer concentration leads to predominantly or all fibers. Therefore, the appearance of the pearls on a string is a transition phase.

If a drug (for example, penicillin) does not bind or interact with an electrospun matrix material, the drug can be entrapped in PGA or PLA pellets or electroaerosoled to produce pellets in the electrospun material. The pellets or electroaerosoled droplets containing the drug begin to dissolve after administration to deliver the entrapped material. Some agents can be coupled to synthetic, or natural polymer by a covalent bond, prior to or after spinning.

In other embodiments, the substance is electroprocessed. Substances can be electroprocessed from the same orifice as the materials or from different orifices. Substances can also be subjected to the same or a different type of electroprocessing as the material. A molecule can be bonded to the electroprocessed material directly or through linking to a molecule that has an affinity for the material. An example of this embodiment involves bonding polypeptide substances to heparin, which has an affinity for collagen materials. This embodiment allows release rate to be controlled by controlling the rate of degradation of the material, for example by enzymatic or hydrolytic breakdown.

In other embodiments, the electroprocessed material can entrap substance during the electrodeposition process. This can be accomplished by disposing substances in the space between the source of the electroprocessed stream and the target for the electroprocessed material. Placing such substances in the space between the source and target can be accomplished by a number of methods, including but not limited to, suspending in air or other gases, dripping, spraying, or electroprocessing the substances. The substances can be present in that space in, for example, particulate, aerosol, colloidal, or vapor form. In these embodiments, the electroprocessed material or matrix will physically entrap the substances. This embodiment can also be used to encapsulate larger particles, such as cells, large particles, or tablets. For example, if a tablet is dropped through the matrix as it forms, the tablet is surrounded by the matrix. If a small object, like a cell is dropped through the matrix as it forms or placed in an aerosol within the matrix, the object may be trapped between filaments, within filaments or "attached to the outside of the filaments. For example, by suspending cells in a solution or within a matrix, the cells can become part of an electrospun matrix during fabrication of the filaments. Alternatively, encapsulation can occur by dropping substances onto or through a matrix material stream as a matrix forms. The cells thus become surrounded by a matrix of electroprocessed material. These embodiments can be used to incorporate within a matrix substances that

are not soluble and/or are too large to form a suspension in the solvent used for the production of the material. For substances in a mist or vapor form, controlling distribution and composition of substances in the space between the source and target can be used to alter the physical and chemical properties of the electroprocessed material and the pattern of distribution of the substances in the electroprocessed material. For all of the foregoing embodiments, the substances can be placed in the electroprocessed material in capsules, vesicles, or other containments for subsequent release. Since the solvent carrier often evaporates in the electroprocessing technique as the electroprocessed material forms, such as a filament, substances may be placed in the electroprocessed matrix and solvent toxicity is greatly reduced or eliminated.

In embodiments wherein the substance comprises cells, the cells can, for example, be suspended in a solution or other liquid that contains the material to be electroprocessed, disposed in the area between the solutions and target, or delivered to a target or substrate from a separate source before, during, or after electroprocessing. Cells can be dripped through the matrix, onto the matrix as it deposits on the target or suspended within an aerosol as a delivery system for the cells to the electroprocessed material. The cells can be delivered in this manner while the matrix is being formed. As an example, cardiac fibroblasts were suspended in phosphate-buffered saline (PBS) at a concentration of approximately one million cells per milliliter. The suspension of cells was placed within a reservoir of a Paasche air brush. To test the efficacy of using this type of device to deliver cells, the cell suspension was initially sprayed onto a 100 mm culture dish. Some of the cells survived, attached to the dish and spread out over the substratum. In a second trial, the culture dish was located further away from the air brush and the experiment was repeated. Cells were observed on the dish. They appeared to be flattened by the impact and were partially spread out over the surface of the substratum. Culture media was added to the dish and the cells were placed into an incubator. After one hour of culture, the cells were inspected again, and many were found to have spread out further over the substratum. These results demonstrate that a simple airbrush device can be used to place cells into an aerosol droplet and deliver them on demand to a surface or site of interest. Cell viability can be improved by restricting this technique to cells that are resistant to the shear forces produced in the technique, developing a cell suspension with additives that cushions the cells or refining the aerosolizing